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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/705,432	11/10/2003	Wojtek Auerbach	REG 784	4884

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EXAMINER	
MONTANARI, DAVID A	
ART UNIT	**PAPER NUMBER**
1632	

MAIL DATE	DELIVERY MODE
11/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/705,432	AUERBACH ET AL.	
	Examiner	Art Unit	
	David Montanari	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication..
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 10/9/07
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/9/2007 has been entered.

1. Claims 17, 21, 25 and 29 are amended.

2. The rejection of claims 17-32 under 35 USC 112, first parag. new matter is withdrawn.

3. Claims 17-32 are examined in the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 17-32 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Rohozinski et al. (Genesis, 2002, Vol. 32, pgs. 1-7) in view of Tsirigotis et al. (BioTechniques, 2001, Vol. 31, pgs. 120-130) and Ghazizadeh et al. (J. Invest. Dermat., 1998 Vol. 111, pgs. 492-496) for reasons of record in the office actions mailed on 8/28/2006 and 6/5/2007.

Claims 17-32 are drawn to an *in vitro* method of targeting a targeting vector into mouse embryonic stem (ES) cell, comprising introducing into said ES cells a targeting vector comprising a ubiquitin promoter, wherein the targeting vector comprises a drug resistance gene encoding neomycin phosphotransferase, hygromycin phosphotransferase, or puromycin acetyl transferase under control of a ubiquitin promoter, wherein said promoter is the ubiquitin C promoter that is a human, mouse, rat, or bacterial ubiquitin C promoter.

Response to Arguments

Applicant argues in amendment filed 10/9/2007 that the current amendment to the claims renders the instant obviousness rejections moot. Applicant continues that in view of KSR v. Telefex, Inc., A&P Tea Co. v. Supermarket Corp. and Anderson's Black Rock v. Pavement Co., there are significant differences between the pending claims and the art of record cited such that is would not be obvious to one of ordinary skill in the art to make or use the claimed method. Applicant argues that there is no guidance in the art of record to teach that targeting with a ubiquitin promoter-driven drug resistance gene will increase successful targeting at a specific chromosomal location with a PGK promoter-driven drug resistance gene. Applicant continues to argue that they are the first to teach that changing the promoter or controlling expression of a drug resistance gene to a ubiquitin promoter, rather than using a commonly used promoter e.g. a PGK promoter, increases the ratio of targeted ES cell clones to total drug resistant ES cells clones when directed to the same chromosomal location as a commonly used art-recognized promoter. Applicant continues that the claimed method not only increases the number of targeted ES cells over the prior art, but also unexpectedly and significantly increases the number of targeted ES cells bearing the selection marker at the specific chromosomal location

corresponding to the homology arms in comparison to randomly-integrated constructs bearing the marker. These arguments are not persuasive.

Applicant has amended the claims to now recite that the claimed targeting method is increased at least two-fold over a PGK promoter-containing targeting vector having homology arms directing the PGK promoter-containing targeting vector to the same chromosomal location. This newly added limitation is given no patentable weight. The newly added amendment to claims 17, 21, 25 and 29 does not further limit nor define the claimed method and only presents an outcome that is inherent to the claimed method. Examining the phrase "two-fold over" in line 6 of claim 17 in view of Applicants data presented in Table 2 on page 11 of the specification it is readily apparent that this is the case when contrasting the ubiquitin promoter vs. the PGK promoter (that there is at least a 2-fold increase in targeting). If this increase in targeting using the ubiquitin promoter is inherent, then the recent amendment to the claims is not further limiting and again is not patentable. Applicant has contrasted two different promoters and attempted to use the data to further limit the claimed method, however the ordinary artisan would not need to rely on this data in order to come up with or practice the claimed method. Sufficient teachings and motivations are presented in the rejection of record with the art cited that would lead the ordinary artisan to practice the claimed method without any reliance or knowledge of an increase in targeting using the ubiquitin promoter vs. the PGK promoter. Applicant has argued that the claimed method is the product of unexpected results when contrasting the use of the ubiquitin promoter vs. the PGK promoter, however this will always be the case as it is inherent to the use of the ubiquitin promoter. Again, as stated in the previous Final Rejection on pg. 5 mailed on 6/5/2007, the homology arms used in the claimed method have only one purpose, to target

nucleotides in the chromosome. These homology arms combined with the ubiquitin promoter, which the art provides ample motivation to use vs. all other promoters, will target specific chromosomal locations within the genome of a mouse ES cell. Unexpected results are not an issue here because this will always be the case when using the ubiquitin promoter. Thus the rejection is maintained for the reasons above and of record.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Montanari whose telephone number is 1-571-272-3108. The examiner can normally be reached on M-Tr 8-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 1-571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

David A. Montanari, Ph.D.

/Anne-Marie Falk/
Anne-Marie Falk, Ph.D.
Primary Examiner, Art Unit 1632